**Health Innovation Oxford & Thames Valley Maternity Network Guideline: use of antenatal corticosteroids: singletons and multiple births**

**Health Innovation Oxford & Thames Valley Maternity Network Version 1 (updated Nov 2024)**

**Antenatal corticosteroids for fetal lung maturation: evidence behind guideline**

Steroid usage remains under intense scrutiny. Obstetric units have performed well at using them, but as their benefit is largely limited to where they are given within 7 days prior to preterm birth, closer scrutiny on timing is understandable.

The 2022 guideline has been updated in 2024. Since its ratification a similar approach has been adopted in many areas: aiming to give steroids where clearly indicated but limit their use to where there will be most benefit.

Given the poor predictive value of even risk factors such as AEDF or SROM, let alone 'threatened preterm birth', timing the steroids is extremely difficult and our current cross-TV rates of nearly 50% are impressive. Accuracy will be improved by point of care tests integrated into apps that use both multiple risk factors and continuous variables to improve both sensitivity and specificity into (note fetal fibronectin currently N/A, so advise Actim Partus *OR* QUIPP app using cervical length), equating to more at-risk babies receiving steroids appropriately. But even these are still not enough. For instance, the QUiPP app (ref 1) which assess the risk of birth within 7 days, still advises steroids when there is a >5% risk of this: this means that many women will still receive steroids that are not effective.

There are also increasing data suggesting that steroids may cause harm. These are well summarised in the RCOG GTG (ref 2). Neonatal hypoglycaemia, an established risk factor for long term childhood neurological sequelae (ref 3), is more common. This is so even in terms births when steroids were given weeks before (ref 5), but the risk is probably greatest among late preterm and early term births (ref 5). A recent report suggested a 2-fold increase in behavioural problems in children born at term (ref 6). Debate remains about neurodevelopment and cardiovascular sequelae of multiple courses (ref 2,6,7). The 2015 middle and low income trial of steroids (ref 10) suggested increased neonatal mortality and higher maternal infection. These issues have inevitably contributed to the sometimes conflicting published advice/ guidelines.

The use of more sensitive and specific tests (e.g. QUiPP) (ref 1) and more careful timing where iatrogenic preterm birth is anticipated will go some way to improve appropriately timed steroids: a full course <7 days prior to birth. Very high levels of compliance risk multiple repeat courses and this is likely, if not very strictly limited, to cause more harm than good.

For repeat ('rescue') steroids, current meta-analysis suggests an increase in low birthweight but a reduction in respiratory problems (ref 8). It would seem reasonable to ensure they are used in the most preterm, when birth <7 days is highly likely and that parents have been involved in decision making. This has been addressed but the individual clinical scenarios will vary.

The proposed guideline also addresses steroids >34+6 weeks. Given the potential risks of steroids this needed to be considered and following an MDT conversation has been addressed.

**References:**


1.QUiPP app toolkit. https://www.bapm.org/pages/187-quipp-app-toolkit

2. RCOG GTG: https://obgyn.onlinelibrary.wiley.com/doi/epdf/10.1111/1471-0528.17027

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4. McKinzie AH, Yang Z, Teal E, Daggy JK, Tepper RS, Quinney SK, et al. Are newborn outcomes different for term babies who were exposed to antenatal corticosteroids? Am J Obstet Gynecol. 2021;225(5):536 e1- e7.

5. Gyamfi-Bannerman C, Thom EA, Blackwell SC, Tita AT, Reddy UM, Saade GR, et al. Antenatal Betamethasone for Women at Risk for Late Preterm Delivery. N Engl J Med. 2016;374(14):1311-20.

6. Raikkonen K, Gissler M, Kajantie E. Associations Between Maternal Antenatal Corticosteroid Treatment and Mental and Behavioral Disorders in Children. JAMA. 2020;323(19):1924-33.

7. NICE: https://www.nice.org.uk/guidance/ng25/resources/preterm-labour-and-birth-pdf-1837333576645

8. Crowther CA, Middleton PF, Voysey M, Askie L, Zhang S,Martlow TK, et al. Effects of repeat prenatal corticosteroids givento women at risk of preterm birth: an individual participant datameta-analysis. PLoS Med.2019;16:e1002771

9.McGoldrick et al 2021. Cochrane. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004454.pub4/epdf/full

10. Althabe et al. A population-based, multifaceted strategy to implement antenatal corticosteroid treatment versus standard care for the reduction of neonatal mortality due to preterm birth in low-income and middle-income countries: the ACT cluster-randomised trial. The Lancet. 2015;385(9968):629-39

**Dose: 12mg betamethasone or dexamethasone, repeated 24 hours later. Only repeat earlier (at 12 hours) if birth likely <24 hours of first dose.**

**1. 22+0[1]-34+6 weeks: indications for recommending [2]:**

| | | |
|---|---|---|
| Threatened PTL: | If QUiPP [3] app suggests >5% risk of birth < 7days. | |
| | If clinically in active labour (cx effaced and regular, painful contractions) | |
| Preterm SROM: | If confirmed by speculum | |
| | If good history and POC test + (not if poor history [4] of SROM and POC test +) | |
| FGR/PET<34w: | If <32w: | at diagnosis of AREDF [5] (deliver by 32w) |
| | | or abnormal antenatal CTG (decelerations or STV<4[6]) |
| | If 32+0-34+6: | if umbA >95$^{th}$ c and EFW <3$^{rd}$ c [7] |
| | | if birth planned <34+6 weeks |
| Other: | Maternal sepsis: ensure adequate resuscitation and IV antibiotics given first[8]. Birth must not be delayed to allow steroids 'to work' | |
| | Consider if other serious maternal illness, admitted for severe pre-eclampsia (beware pulmonary oedema) | |
| | Bulging membranes; significant PVB, severe abdominal pain etc | |
| | <1 week before any planned CS <34+6 weeks | |
| >7 days since steroids: | A single 'repeat course' should be considered if > 7 days since first course, if birth <30+0 is planned or *highly likely* to be <7 days [9]. The risks/ benefits should be discussed with the parents. | |

**2. >34+6 <37+0: recommend steroids if:[10]**

| | |
|---|---|
| Fetal lung issue: | Specifically, fetal lung abnormality/cardiac problem likely to cause lung issues. Give for all indications as above (i.e. if birth anticipated at <37+0 in <7 days) |
| Pre-labour CS, <37+0: | <1 week before any planned CS <37+0 weeks |
| Other indications: | (i.e. all above: section 1 and birth anticipated at <37+0 in <7 days.) Recommend RCOG based decision tool[8] for all above indications and *only give if* parents request. This includes women with diabetes or GDM. |
| >7 days since steroids | repeat not advised |

**3. >36+6<39+0 weeks: recommend steroids If [10]:**

| | |
|---|---|
| Fetal lung issue: | Specifically, fetal lung abnormality/cardiac problem likely to cause lung issues. Give for all indications (i.e. if birth anticipated at <39+0 in <7 days) |
| Other indications: | Not advised. This includes women with diabetes or GDM. |
| >7 days since steroids | repeat not advised |

**Notes:**

1. Wait for 22+0
2. From 22+0 weeks-26+6 weeks (or twins 27+6 weeks or any EFW <800g) IUT to Level 3 NNU advised if criteria for steroids met/parents wish active intervention. Also consider MgSO4 if birth likely <12 hours.
3. QUiPP app ('symptomatic' part) has better sensitivity and specificity: meaning better timing. Unavailability of fFn means it cannot be used, incl as part of QUiPP app. NHSE recommend Actim Partus instead or using the QUiPP app integrating cervical length scan. Risk high= QUIPP app risk <7 days >5% OR Actim Partus positive
4. False positive rates of POC tests can be high.
5. AREDF usually lasts for several days before there is decompensation particularly in more preterm fetuses. Note steroids may be followed by temporary return of EDF
6. Delivery likely within 48 hours if present and AEDF not always present before decompensation. STV <3 a criterion for delivery <24 hours under most circumstances
7. At this gestation AREDF is indication for birth: these criteria suggest high risk of birth <7 days
8. WHO recommendation against giving steroids where 'chorioamnionitis'. Based on data from non-high income countries. Given frequency of chorioamnionitis, usually subclinical, with preterm birth this appears to contradict data from populations more relevant to the UK.
9. This is controversial but given increased mortality risk without steroids, benefits probably > risks, particularly at extreme preterm gestations. https://journals.plos.org/plosmedicine/article/file?id=10.1371/journal.pmed.1002771&type=printable. 30 weeks was chosen as corresponding to average gestation in most trials' participants.
10. At this gestation steroids reduce RDS but this should be set against the risk of hypoglycaemia and probable long term issues in the child. https://obgyn.onlinelibrary.wiley.com/doi/epdf/10.1111/1471-0528.17027.